Clinical Update

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Regenerative Endodontics: Part 2

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Introduction

Regenerative endodontic procedures are biologically based and designed to replace damaged dentin, root and cells of the pulp-dentin complex (1). This encompasses simple blood clot revascularization to the complex, emerging field of tissue-engineered pulp (2). The goal is to regenerate pulp and dentin, restore function, foster root development and prevent or resolve apical periodontitis (3). The aim of this clinical update is to review current clinical procedures for managing diseased or traumatized pulps of permanent teeth with immature root apices and discuss implanting engineered pulp into cleaned and shaped root canals. "Growing teeth" is beyond the scope of this paper and can be addressed in a future clinical update.

Management of the immature root apex

Calcium hydroxide (CH) placement into a root canal is used to induce calcific barriers at the immature root apex. Mineral trioxide aggregate (MTA) has osteoinductive properties and sets in the presence of moisture. Many advocate a single visit apexification procedure with MTA for results more predictable than CH (4). Apexification requires prolonged treatment time, does not allow for further root development and leaves thin dentinal walls, increasing risk of root fracture (5-7).

Revitalization or regeneration of pulp tissue in the canal would lead to stronger teeth (4). Retrospective studies (8), prospective clinical studies (9) and case reports (10,11) utilizing a blood clot revascularization technique have promising outcomes characterized by the absence of clinical disease, regression of an apical lesion and continued root development. Figure 1 is the treatment protocol proposed by Banchs and Trope (12) using a triple antibiotic paste tested by Hoshino et al. on root canal bacteria (13). A disadvantage of this therapy is tooth discoloration to a bluish-grey hue (14). Minocycline in the antibiotic mixture may be responsible for the discoloration, but the outcome is not consistent (11). Patients and parents/guardians should be advised of potential staining and a subsequent need for bleaching. After 3 months, if there are no radiographic signs of regeneration, apexification or nonsurgical root canal treatment can be initiated (12). Petrino et al. suggested treatment modifications including using anesthetic without a vasoconstrictor (mepivacaine) to help induce bleeding into the canal space. They also used a collagen product such as CollaPlug® (Dentsply Tulsa Dental, Tulsa, OK) as a barrier over the clot to contain the MTA (11). Omitting minocycline from the paste is suggested to reduce staining, but the paste's antimicrobial effect without minocycline is unknown. Recently, Wang et al. described the phenotype of regenerated tissue in a canal space as cementum-like, bone-like and PDL-like tissue. It was not of parenchymal origin, therefore revitalization in that study may have been more appropriately described as wound healing, not pulpal regeneration (15).

Access preparation
↓
Irrigate canal (20ml 6% NaOCl and 10ml 0.12% chlorhexidine)
↓
Paper point dry canal
↓
Place antibiotic paste* (3Mix-MP) in canal
↓ ***(4 weeks)***
Confirm absence of exudates, irrigate canal (10ml 6%NaOCl)
↓
Gently probe canal to induce bleeding
↓
Allow clot to form below the CEJ
↓
Place MTA, wet cotton pellet and Cavit® over clot
↓ ***(2 weeks)***
Replace Cavit® with a definitive restoration

Figure 1. Treatment regimen for necrotic pulps in immature permanent teeth (12).

*To make the 3Mix-MP antibiotic paste, remove the sugar coating from 1tablet each of 200mg Ciprofloxacin, 500 mg Metronidazole, and 100mg Minocycline with a surgical blade and crush each individually in separate mortars. Capsules must be opened in separate mortars and ground to a fine powder. Equal amounts of antibiotics (1:1:1) should be combined on a mixing pad. For the carrier, use equal amounts of macrogol ointment and propylene glycol and mix on a pad using a clean spatula. This should result in an opaque mixture. Small portions of the 3Mix antibiotics should be incorporated in the carrier in a 1:5 carrier to 3Mix ratio, resulting in a creamy consistency (12). Incorporating a radioopacifier, such as barium sulfate, into the mix is optional.

AAE Registry

The American Association of Endodontists has established a regenerative endodontics database. It is open for all AAE members to submit information. The goal is to help establish a best treatment practice for the immature tooth with a necrotic pulp. To access the registry log on to www.aae.org, follow the tab to "Publications & Research", scroll down to "Regenerative Endodontics" and follow the instructions. Ob-

tain patient consent prior to electronically uploading de-identified radiographs into the database. Case submission takes 10-15 minutes.

Reengineering pulp

Methods which allow for the delivery of known cells, signaling molecules and scaffolds into a root canal space for tissue engineering are being studied (3). Pulp tissue engineering uses progenitor cells of endodontic origin. These pulp constructs could optimally support continued root development. One in vivo study found that stem cells from exfoliated deciduous teeth (SHED) seeded in tooth slice/scaffolds were stimulated to differentiate into dentin secreting odontoblast-like cells along the dentin surface. These SHED cells were capable of forming microvascular networks (16). Implanted stem cells and growth factors accelerated the process of differentiation, proliferation and migration to induce pulpal healing (17). Autologous stem cells are the best source of stem cells, with cell and tissue banking a viable option for later use (18). Components of the tissue engineering triad (dental pulp stem cells (DPSC), collagen scaffolds and growth factors) discussed in Part 1 of this clinical update were found to induce regeneration when transplanted in human dentin slices implanted in immunodeficient mice (19).

Choosing a proper irrigant to chemically debride the root canal space prior to implanting engineered tissue is also important. Dentinal walls must support cell colonization. Sodium hypochorite use will likely be contraindicated. There are ongoing investigations of the biocompatibility of endodontic irrigants that allow for preservation of growth factors on dental surfaces and promote odontoblast colonization. Recently, antimicrobial agents such as fruit juice from the *Morinda citrifolia* plant (Hawaiian noni) and *Aquatine EC* (hypochlorous acid) have supported DPSC survival and attachment to dentin (20, 21). Likewise, whether or not to remove the smear layer from a root canal is controversial. Smear hindered the adherence of implanted stem cells to dentin in one study (1). In another, DPSC attached to dentinal tubules and the smear layer, suggesting that removal may not be needed for regenerative therapy (21).

Conclusion

Research and clinical developments have changed the protocol for treating immature, permanent teeth with necrotic pulps. Revitalization therapy offers advantages including shorter overall treatment time, infection control, cost effectiveness, root lengthening and hard tissue deposition. However, an uncomplicated clinical procedure using stem cell-based endodontic therapy has not yet been established. Continuous efforts to develop a regimen for tissue engineering of the pulp-dentin complex promise to revolutionize dentistry.

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